FBXL4 Gene

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F-box and leucine rich repeat protein 4

genes

1. Normal Function

The *FBXL4* gene provides instructions for making a member of a family of proteins called F-box and leucine rich repeat proteins. Like other members of this family, FBXL4 associates with a group of proteins to form a complex. The protein complex that contains FBXL4 is found within cell structures called mitochondria. Mitochondria are involved in a wide variety of cellular activities, including energy production, chemical signaling, and regulation of cell growth and division (proliferation) and cell death (apoptosis). Mitochondria contain their own DNA, known as mitochondrial DNA (mtDNA), which is essential for the normal function of these structures. As part of the protein complex, the FBXL4 protein is likely involved in the maintenance of mtDNA. Having an adequate amount of mtDNA is essential for normal energy production within cells.

2. Health Conditions Related to Genetic Changes

2.1 FBXL4-Related Encephalomyopathic Mitochondrial DNA Depletion Syndrome

More than 47 mutations in the *FBXL4* gene have been found to cause *FBXL4*-related encephalomyopathic mtDNA depletion syndrome. This condition affects multiple body systems and is often fatal in early childhood. It is primarily associated with brain dysfunction combined with muscle weakness (encephalomyopathy).

Many of the mutations that cause *FBXL4*-related encephalomyopathic mtDNA depletion syndrome impair the FBXL4 protein's ability to attach (bind) to other proteins, disrupting the formation of the protein complex, which impairs normal maintenance of mtDNA. Problems with mtDNA maintenance can reduce the amount of mtDNA (known as mtDNA depletion). Depletion of mtDNA impairs mitochondrial function in many of the body's cells and tissues. Reduced mitochondrial function eventually leads to cell dysfunction, most noticeably affecting the brain, muscles, and other tissues that have high-energy requirements. This cell dysfunction leads to encephalomyopathy and other features of *FBXL4*-related encephalomyopathic mtDNA depletion syndrome.

2.2 Leigh Syndrome

3. Other Names for This Gene

- F-box/LRR-repeat protein 4
- FBL4
- FBL5

References

1. Almannai M, Dai H, El-Hattab AW, Wong LJC. FBXL4-Related EncephalomyopathicMitochondrial DNA Depletion Syndrome. 2017 Apr 6. In: Adam MP, Ardinger HH, PagonRA, Wallace SE, Bean LJH, Stephens K, Amemiya A, editors. GeneReviews®[Internet]. Seattle (WA): University of Washington, Seattle; 1993-2020. Availablefrom http://www.ncbi.nlm.nih.gov/books/NBK425540/
2. Bonnen PE, Yarham JW, Besse A, Wu P, Faqeih EA, Al-Asmari AM, Saleh MA, Eyaid W, Hadeel A, He L, Smith F, Yau S, Simcox EM, Miwa S, Donti T, Abu-Amero KK, WongLJ, Craigen WJ, Graham BH, Scott KL, McFarland R, Taylor RW. Mutations in FBXL4cause mitochondrial encephalopathy and a disorder of mitochondrial DNAmaintenance. Am J Hum Genet. 2013 Sep 5;93(3):471-81. doi:10.1016/j.ajhg.2013.07.017.Oct 3;93(4):773.
3. Dai H, Zhang VW, El-Hattab AW, Ficicioglu C, Shinawi M, Lines M, Schulze A,McNutt M, Gotway G, Tian X, Chen S, Wang J, Craigen WJ, Wong LJ. FBXL4 defectsare common in patients with congenital lactic acidemia and encephalomyopathicmitochondrial DNA depletion syndrome. Clin Genet. 2017 Apr;91(4):634-639. doi:10.1111/cge.12894.
4. Gai X, Ghezzi D, Johnson MA, Biagosch CA, Shamseldin HE, Haack TB, Reyes A,Tsukikawa M, Sheldon CA, Srinivasan S, Gorza M, Kremer LS, Wieland T, Strom TM,Polyak E, Place E, Consugar M, Ostrovsky J, Vidoni S, Robinson AJ, Wong LJ,Sondheimer N, Salih MA, Al-Jishi E, Raab CP, Bean C, Furlan F, Parini R, LampertiC, Mayr JA, Konstantopoulou V, Huemer M, Pierce EA, Meitinger T, Freisinger P,Sperl W, Prokisch H, Alkuraya FS, Falk MJ, Zeviani M. Mutations in FBXL4,encoding a mitochondrial protein, cause early-onset mitochondrialencephalomyopathy. Am J Hum Genet. 2013 Sep 5;93(3):482-95. doi:10.1016/j.ajhg.2013.07.016.